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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,142	02/18/2004	Stephanos Kyrkanides	21108.0040U1	3987

23859 7590 01/27/2006

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,142	KYRKANIDES, STEPHANOS	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43,72-75,83-91 and 133-141* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-43,72-75,83-91,133-141* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Rejection of June 9, 2005, on November 9, 2005. Claims 1, 84-86 are amended.

Claims 1-43, 72-75, 83-91, 133-141 are under consideration.

Withdrawn Rejections

Double Patenting

Claims 1-43, 72-75, 83-86 were provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-43, 72-75, 83-86 of copending Application No. 10/978,927 ('927). However, claims 1-86 of '927 were cancelled in a claim amendment, filed September 20, 2005. As such, the provisional rejection of claims 1-43, 72-75, 83-86 under 35 U.S.C. 101 is withdrawn.

35 U.S.C. § 101

Applicant's arguments, see pages 15-16 of Applicant's response, filed November 9, 2005, with respect to the rejection of claims 1-43, 84-91, 133-141 under 35 U.S.C. 101 have been fully considered and are persuasive. Applicant has amended the claims to include, "isolated". The rejection of claims 1-43, 84-91, 133-141 has been withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-43, 72-75, 83-91, and 133-141 remain rejected in modified form under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

1) a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes HEX-beta, wherein the sequence is set forth in SEQ ID NO. 3, and wherein the second cistron encodes HEX-alpha, wherein the sequence is set forth in SEQ ID NO. 1.

2) a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes HEX-alpha, wherein the sequence is set forth in SEQ ID NO. 1, and wherein the second cistron encodes HEX-beta, wherein the sequence is set forth in SEQ ID NO. 3.

3) a composition comprising a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes HEX-beta, wherein the sequence is set forth in SEQ ID NO. 3, and wherein the second cistron encodes HEX-alpha, wherein the sequence is set forth in SEQ ID NO. 1.

4) a composition comprising a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes HEX-alpha, wherein the sequence is set forth in SEQ ID NO. 1, and wherein the second cistron encodes HEX-beta, wherein the sequence is set forth in SEQ ID NO. 3.

does not reasonably provide enablement for

any nucleic acid construct or composition comprising a nucleic acid construct comprising a promoter operably linked to a nucleotide sequence comprising two cistrons and a nucleotide sequence that provides IRES activity operably linked to the cistron subsequent to the first cistron, wherein the first cistron encodes any HEX-alpha, other than SEQ ID NO. 1, and wherein the second cistron encodes any HEX-beta, other than SEQ ID NO. 3.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons of record, June 6, 2005.

Applicant's arguments filed November 9, 2005 have been fully considered and they are persuasive in part.

It is noted that the Applicant had indicated that the Examiner had considered the claimed invention (a nucleic acid construct comprising nucleic acid sequences encoding HEXA and HEXB and composition comprising said nucleic acid construct) only in the scope of gene therapy. Applicant has indicated that the scope need not be so limited as

nucleic acid constructs have other applications. As such, the Examiner has reconsidered several of the issues raised in the Office Action of June 9, 2005, and has considered whether the claimed invention could be used in *in vitro* applications.

In light that the claimed invention has uses *in vitro*, the Examiner has taken into consideration that the claimed nucleic acid constructs could be used to express HEXA and HEXB protein. As such, with regard to the issue that the Examiner raised in the Office Action, June 9, 2005, pages 7-8, over whether or not the orientation of the two cistrons relative to the IRES were enabled, the Examiner withdraws the rejection. That is, regardless of whether a protein is expressed weakly or robustly in culture is not an issue of enablement *in vitro*. For this reason, the issue over the selection of an IRES and the orientation of cistrons relative to the IRES is withdrawn.

With regards to the Applicant indicating that the claimed invention is enabled for nucleic acid sequence that encode HEX proteins which are 70-95% identical to SEQ ID NO. 1 or SEQ ID NO. 3 (Applicant's response, page 22), the Examiner does not find the argument persuasive. While it may be true that there are some examples wherein a molecule with 70% or greater homology to a known sequence will have essential physical properties of the identified structure, the problem here is that nothing in the specification or the art provide guidance as to what regions of SEQ ID NO. 1 and SEQ ID NO. 3 need to be conserved in order for the claimed invention to work. That is, what structure(s) of the proteins encoded by SEQ ID NO.1 and SEQ ID NO. 3 would need to be maintained in order for the HEX proteins to have activities. This issue has been addressed as well in the written description rejection (see below). As such, because no

guidance was provided, an artisan does not know how to make and use the proteins encoded by SEQ ID NO. 1 and 3.

With regards to the issue of delivery of HEX constructs (Applicant's response, page 23), the Examiner withdraws the rejection because the claimed invention can be used *in vitro*. Similarly, while the Examiner has applied the enablement issues to *in vivo* situations as it pertains to inducible systems, the Examiner withdraws the rejection.

With regards to the issue of use of promoters in the claimed invention (Applicant's response, page 24), the Examiner finds the argument persuasive. Applicant indicates that a skilled artisan would be able to select a suitable cell-specific promoter using routine techniques. In light of the fact that the claimed invention has *in vitro* applications, the rejection as it applies to the scope of promoters is withdrawn.

With regards to the issue of vectors in the claimed invention (Applicant's response, page 26), the Examiner withdraws the rejection because enablement rejection as they applied to the non-viral and viral vectors was based on an *in vivo* scope.

In summary, claims 1-43 72-75, 83-91, and 133-141 remain rejected as nothing in the art or specification provide guidance for an artisan to practice the claimed invention for its fullest breadth of any HEX-alpha or HEX-beta, other than that of SEQ ID NOs. 1 and 3.

Claims 1-43 72-75, 83-91, and 133-141 remain rejected in modified form under 35 U.S.C. 112, first paragraph, as failing to comply with the written description

requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record, June 9, 2005.

Applicant's arguments filed November 9, 2005 have been fully considered but they are not persuasive in part.

Applicant indicates that the art teaches that it is generally understood that a molecule with 70% or greater homology to a known sequence will have the essential physical properties of the identified structure (Applicant's response, page 30). The Examiner does not find this argument persuasive because as indicated in the Office Action, June 9, 2005, pages 20-23, the reason why a protein sequence with 70% homology may generally be functional, is because much of the structure(s) that contribute to the protein's function is conserved. The issue at hand is that nothing in the art or specification provides structural and corresponding functional characteristics of HEXA and HEXB protein such that an artisan can obtain mutants of HEXA and HEXB and know whether or not they have activity. As such, the claimed invention is enabled for the nucleic acid sequences of human HEXA and human HEXB (SEQ ID NOs. 1 and 3). With regards to the promoters and IRESes, the issue of written description has been withdrawn as the claimed invention has uses *in vitro*. An artisan would know what promoters to use in different cell types *in vitro*. With regards to IRESes, the art teaches many different kinds of IRES which an artisan could use in the claimed invention,

regardless of whether the IRES can be used to translate protein robustly is not an issue *in vitro*.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

DAVE TRONG NGUYEN
SUPERVISORY PATENT EXAMINER